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CORRESPONDENCE

Letters to the Editor

Aspirin for Prevention of Myocardial Infarction and Stroke

Is the Right Dose 81 or 160 Mg/Day?

The recent Expert Consensus Document on Reducing the Gastrointestinal Risks of Antiplatelet Therapy and NSAID Use (1) recommends that the appropriate dose of aspirin (ASA) for cardioprophylaxis is 81 mg/day. Many of the 50 million Americans who take ASA for cardioprophylaxis have been advised to take larger doses: 160 or 325 mg/day. Should they be advised to decrease their dose to 81 mg/day?

I believe that this document (1) underestimates the impact of the dosage of ASA on its ability to prevent myocardial infarction (MI) and stroke.

There is considerable evidence from 4 primary prevention trials that doses <160 mg/day may fail to prevent MI and stroke. ASA, 50 mg/day, failed to prevent MI in the Women's Health Study (2), 75 mg/day failed to prevent MI in women in the HOT (Hypertension Optimal Treatment) study (3), and 100 mg/day failed to prevent MI in men or women in the Primary Prevention Project (4). The findings were similar for the primary prevention of stroke in these randomized trials. With the exception of the Women's Health Study (2), which reported a 17% reduction in stroke ($p = 0.04$), stroke was not decreased in the HOT study (3) or the Primary Prevention Project (4). In a primary prevention trial in patients with type 2 diabetes, Ogawa et al. (5) reported that ASA 81 or 100 mg/day did not decrease the incidence of stroke or MI.

I also believe that this document overestimates the impact of the dosage of ASA on the incidence of its major complication: upper gastrointestinal (UGI) bleeding. Their recommendation is based, in part, on a paper by Weil et al. (6) that reported that the odds ratio (OR) of UGI bleeding in elderly patients with daily doses of ASA of 75, 150, and 300 mg/day were 2.3, 3.2, and 3.9, respectively. This study (6) involved only 144 patients with UGI bleeding. Only 27 patients took ASA 75 mg/day, and 22 took 150 mg/day. Given the wide confidence intervals in this small study, the differences in the ORs of UGI bleeding in the dose range of 75 to 300 mg/day were not significantly different.

In another report that they cited, Sorensen et al. (7) reported the findings in 27,694 ASA users who were hospitalized for UGI bleeding. The OR of UGI bleeding in 6,084 patients taking ASA 100 mg/day was exactly the same as the OR in the 22,671 patients taking 150 mg/day. In a meta-analysis by Serebruany et al. (8) of the bleeding complications in 50 randomized controlled trials of ASA therapy in 338,191 patients, the incidence of major bleeding was the same in 13,337 taking <100 mg/day as in 43,489 patients taking 100 to 325 mg/day (1.7%).

There is no evidence that the risk of UGI bleeding is increased in patients who take ASA 160 mg/day compared with those who take 81 mg/day. There is considerable evidence that ASA doses <160 mg/day are less effective in the primary prevention of stroke and MI. Until contrary data emerge, I will continue to recommend ASA 160 mg/day for the primary prevention of MI and stroke (9).

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REFERENCES

1. Bhatt DL, Scheiman J, Abraham NS, et al. ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID use. J Am Coll Cardiol 2008;52:1502–17.
2. Ridker PM, Cook NR, Lee IM, et al. A randomized trial of low-dose aspirin in the primary prevention of cardiovascular disease in women. N Engl J Med 2005;352:1293–304.
3. Hansson L, Zanchetti A, Carruthers SG, et al. Effects of intensive blood-pressure lowering and low dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. Lancet 1998;351:1755–62.
4. Collaborative Group of the Primary Prevention Project (PPP). Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice. Lancet 2001;357:89–95.
5. Ogawa H, Nakayama M, Morimoto T, et al. Low-dose aspirin for primary prevention of atherosclerotic events with type 2 diabetes. JAMA 2008;300:2134–41.
6. Weil J, Colin-Jones D, Langman M, et al. Prophylactic aspirin and risk of peptic ulcer bleeding. BMJ 1995;310:827–30.
7. Sorensen HT, Mellemkjaer L, Blot WJ, et al. Risk of upper gastrointestinal bleeding with use of low-dose aspirin. Am J Gastroenterol 2000;95:2218–24.
8. Serebruany VL, Malinin AI, Eisert RM, et al. Risk of bleeding complications with antiplatelet agents: meta-analysis of 338,191 patients enrolled in 50 randomized controlled trials. Am J Hematol 2004;75:40–7.
9. Dalen JE. Aspirin to prevent heart attack and stroke: what's the right dose? Am J Med 2006;119:198–202.

Reply

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